**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION**
**DECISION SUMMARY**
**DEVICE ONLY TEMPLATE**

**A. 510(k) Number:**
k041596

**B. Purpose for Submission:**
New Device

**C. Analyte:**
Creatine Kinase Isoenzyme MB (CK-MB) and calibrators

**D. Type of Test:**
Quantitative, Chemiluminescent Microparticle Immunoassay (CMIA)

**E. Applicant:**
Fisher Diagnostics

**F. Proprietary and Established Names:**
ARCHITECT® STAT CK-MB Immunoassay and ARCHITECT STAT CK-MB Calibrators A-F

**G. Regulatory Information:**

1. Regulation section:
   21 CFR 862.1215
   Creatine Phosphokinase/ Creatine Kinase or Isoenzymes Test Systems
   21 CFR 862.1150
   Calibrator

2. Classification:
   Class II

3. Product Code:
   JHX Creatine phosphokinase/creatine kinase or isoenzymes test system
   JIS Calibrator, Primary

4. Panel:
   75 Clinical Chemistry

**H. Intended Use:**

1. Intended use(s):
   ARCHITECT® STAT CK-MB is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of CK-MB in human

serum and plasma on the ARCHITECT i System with STAT capability. CK-MB values are used to assist in the diagnosis of myocardial infarction (MI).

2. Indication(s) for use:
   See intended use above.

3. Special condition for use statement(s):
   For Prescription Use.

4. Special instrument Requirements:
   ARCHITECT® i System

**I. Device Description:**

ARCHITECT® STAT CK-MB is a 2-step quantitative chemiluminescent microparticle immunoassay that determines the presence of the MB isoenzyme of creatine kinase (CK-MB) in human serum and plasma.
The device uses 2 reagents that are provided as microparticles, anti-CK-MB (mouse monoclonal coated microparticles in TRIS buffer) and conjugate anti-CK-MB (mouse monoclonal acridinium conjugate in MES buffer in protein). Also, the device uses calibrators and controls (controls already cleared k040880). Trigger and pre-trigger solutions and wash buffers are not provided with the conjugate and microparticles. The calibrators will be received in the starter reagent kit and can be purchased separately.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):
   Abbott AxSYM® CK-MB Assay

2. Predicate K number(s):
   k935924

3. Comparison with predicate:

| Similarities | | |
|---|---|---|
| **Item** | **Device** | **Predicate** |
| Intended Use | ARCHITECT Stat CK-MB is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of creatine kinase (CK-MB) in human serum and plasma on the ARCHITECT i System with STAT capability. CK-MB values are used to assist in the diagnosis of myocardial | The AxSYM CK-MB is a microparticle enzyme immunoassay (MEIA) for the quantitative measurement of the MB isoenzyme of creatine kinase (CK-MB) in human serum and plasma using the AxSYM immunoassay systems to aid in the diagnosis and treatment of |

| | | |
|---|---|---|
| | infarction (MI). | myocardial infarction. |
| Components | • Microparticles: Anti-CK-MB (mouse, monoclonal) coated microparticles in TRIS buffer with protein (bovine) stabilizers.<br>• Conjugate: Anti CK-MB (mouse, monoclonal) acridinium conjugate in MES buffer with protein (bovine) stabilizer.<br>• Trigger and Pre-trigger Solutions<br>• Wash Buffer<br>• Calibrators A-F<br>• Controls (K040880) | • Microparticles: Anti-CK-MB (mouse, monoclonal) coated microparticles in TRIS buffer.<br>• Conjugate: Anti CK-MM (goat) Alkaline Phosphatase in TRIS buffer with protein stabilizers.<br>• Assay Diluent containing goat serum with protein stabilizers.<br>• Calibrators A-f along with 2 master calibrators.<br>• Controls |
| Storage | Reagents at 2-8º C<br>Calibrators at -10º C | 2-8º C |
| **Differences** | | |
| **Item** | **Device** | **Predicate** |
| Instrumentation Required | ARCHITECT i System | AxSYM System |
| Test Principle | Chemiluminescence Microparticle Immunoassay (CMIA) | Microparticle Enzyme Immunoassay (MEIA) |

**K. Standard/Guidance Document Referenced (if applicable):**

NCCLS' standard, "C28-A2: How to Define and Determine Reference interval in the Clinical"
NCCLS's "EP7-A: interference Testing in Clinical Chemistry"
NCCLS' standard, "EP5-A: Evaluation of Precision Performance of Clinical Chemistry".
FDA Document Shelf Life of Medical Devices in April 1991
HIMA Stability Testing Programs for In Vitro Diagnostic Products July 1983
NCCLS standard, "EP9-A2: Method Comparison and Bias Estimation Using Patient Samples".

**L. Test Principle:**

ARCHITECT Stat CK-MB immunoassay uses two steps to determine the presence of creatine kinase MB isoenzyme in human serum or plasma. The first step is

combining the sample with the anti CK-MB coated paramagnetic particles which is followed by incubation and washing. In the second step, the anti CK-MB acridinium conjugate is added. The pre-trigger and trigger solutions are added to produce a chemiluminescent reaction. This reaction is measured in relative light units (RLUs). The ARCHITECT i System is an optical system that is capable of measuring the amount of CK-MB in a serum or plasma sample based on the RLUs.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

*a. Precision/Reproducibility:*

Three lots of reagent assay were run in replicates of two at two separate times per day for twenty days on two instruments to determine reagent lot differences and variation in controls (low, medium and high). All three lots met their acceptance criteria and the total imprecision CV ranged between 2.9% to 5.0 %.

*b. Linearity/assay reportable range:*

Ten patient samples with analyte concentrations between 190.50 and 300.00 ng/mL were diluted with human plasma to obtain the lower end of the detection. The diluted samples ranged between 5.3 to 275 ng/mL. The dilution linearity of ARCHITECT Stat CK-MB immunoassay met their acceptance criteria of +/- 20 % of the undiluted CK-MB concentration with a mean of 100.4 % recovery and a range from 92.9% to 106%.

*c. Traceability (controls, calibrators, or method):*

No traceability was provided.

Each starter kit included the calibrators A-F as well as sold separately as a calibrator kit. The calibrators in the ARCHITECT Stat CK-MB calibrator kit are used for the calibration of the ARCHITECT i System when used for the quantitative determination of CK-MB in human serum and plasma.

Calibrator A contains MOPS (3-(N-Morpholino)-propanesulfonic acid) buffer with protein stabilizer. Calibrators B-F contain recombinant CK-MB in MOPS buffer with protein (bovine) stabilizer.

| | |
|---|---|
| CAL A- 0.00 ng/mL | CAL D- 60.0 ng/mL |
| CAL B- 3.8 ng/mL | CAL E- 135 ng/mL |
| CAL C- 12.0 ng/mL | CAL F- 300 ng/mL |

Stability:

Calibrator stability studies were conducted (stress, open and closed vial) on three lots of calibrators from the ARCHITECT Stat CK-MB immunoassay. Storage of the calibrators at 30º C demonstrated stability of 5.8 weeks. The open vial stability demonstrated acceptable stability for 30 days at 2-8 C. Accelerated studies, along

with real-time intended storage (-10 C) and real-time at intended thawed condition (2-8º C) confirm their dating of 12 months.

*d. Detection limit:*

The assay detection range is 0.1 ng/mL to 300 ng/mL. Assays on samples >300 ng/mL are flagged with a code by the ARCHITECT i System and may be diluted (1:2) with automated or manual procedures as per the ARCHITECT i System manual.
The ARCHITECT STAT CK-MB analytical sensitivity <0.1 ng/mL at the 95% level of confidence (38 runs and 10 replicates of Calibrator A and 4 replicates of Calibrator B per run). Analytical sensitivity is defined as the concentration at two standard deviations above the ARCHITECT STATE CK-MB calibrator A (0.1 ng/mL) grand mean and represents the lowest concentration of CK-MB that can be distinguished from zero.
The calibration range is 0.0 to 300.00 ng/mL. In the labeling, it is recommended that a single sample of all levels of CK-MB controls be tested to evaluate the assay calibration.

*e. Analytical specificity:*

Potentially cross-reactive substances were evaluated by spiking different concentrations of CK-MB using NCCLS's "EP7-A: Interference Testing in Clinical Chemistry". One lot and instrument were used to determine the interferences of Bilirubin (20 mg/dL), Hemoglobin (500 mg/dL), triglycerides (1000 mg/dL) and total protein (4 and 10 g/dL) using high and low interference levels. The % interference was evaluated using the equation:

$$\% \text{ interference} = \frac{(\text{Test conc.} - \text{Control Conc.})}{\text{Control Conc.}} \times 100$$

The compounds appear to have no significant cross reactivity (<10%) with the ARCHITECT Stat CK-MB immunoassay and reflected values of between -3.7% and 1.7% percent interference.

A total of 10 sample pairs were tested for HAMA interference and 10 sample pairs were tested for RF interference using one reagent lot and one instrument system according to the guidelines from NCCLS EP7. The amount of interference for HAMA was less than 15% based on actual and absolute values. The average absolute HAMA interference was 5.58% with a range of 1.53% to 11.8%. The amount of interference for RF was less than 10% based on actual and absolute values. The average absolute RF interference was 3.85% with a range of 0.61% to 8.37%.

*f. Assay cut-off:*

N/A

2. Comparison studies:
    a. *Method comparison with predicate device:*
    251 serum and plasma samples were tested on both the Architect and AxSYM CK-MB assays. 13 samples were excluded because they were below the sensitivity of the of the predicate devices sensitivity range. Of the remaining 238 samples, 24 required dilution and were thus excluded. The remaining 13 serum specimens of the remaining 214 specimens were further excluded in order to have a consistent tube type (Lithium Heparin) in the correlation analysis.
    The Passing-Bablok regression analysis was conducted on the remaining 201 undiluted plasma samples only. The Architect assay ranged from 1.5 to 256.9 ng/mL and the AxSYM ranged from 1.8 to 296 ng/mL. The regression analysis obtained a y-intercept of -.512 (95% CI of -1.160 to 0.139), slope of 0.808 (95% of 0.786 to 0.824) and a correlation coefficient (r) of 0.985.

    b. *Matrix comparison:*
    A serum and plasma comparison study was conducted to compare tube interference. Interference from all the plasma tubes- Sodium Heparin, Plasma Separator (glass and plastic) and Lithium Heparin showed interference of 1.6%, 1.2% 1.4% and 7.0% respectively. Whereas, the Serum (uncoated glass) and Serum Separator (plastic) showed interference of 13.5% and 10.7% respectively.

3. Clinical studies:
    a. *Clinical sensitivity:*
    N/A
    b. *Clinical specificity:*
    N/A
    c. *Other clinical supportive data (when a and b are not applicable):*
    N/A

4. Clinical cut-off:
    N/A

5. Expected values/Reference range:
    300 specimens from donors were tested with the ARCHITECT STAT CK-MB to establish a normal range from normal population.
    The 99$^{th}$ percentile concentration for serum and plasma specimens is 6.3 ng/mL and 6.4 ng/mL, respectively. The 99$^{th}$ percentile concentration for plasma male and female specimens is 7.2 ng/mL and 3.4 ng/mL, respectively. Guidelines and principles from NCCLS' standard, "C28-A2: How to Define and Determine Reference Intervals in the Clinical Laboratory" was used.

**N. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.